

# Stuttering

## Clinical and research update

Hector R. Perez MDMS James H. Stoeckle

### Abstract

**Objective** To provide an update on the epidemiology, genetics, pathophysiology, diagnosis, and treatment of developmental stuttering.

**Quality of evidence** The MEDLINE and Cochrane databases were searched for past and recent studies on the epidemiology, genetics, pathophysiology, diagnosis, and treatment of developmental stuttering. Most recommendations are based on small studies, limited-quality evidence, or consensus.

**Main message** Stuttering is a speech disorder, common in persons of all ages, that affects normal fluency and time patterning of speech. Stuttering has been associated with differences in brain anatomy, functioning, and dopamine regulation thought to be due to genetic causes. Attention to making a correct diagnosis or referral in children is important because there is growing consensus that early intervention with speech therapy for children who stutter is critical. For adults, stuttering can be associated with substantial psychosocial morbidity including social anxiety and low quality of life. Pharmacologic treatment has received attention in recent years, but clinical evidence is limited. The mainstay of treatment for children and adults remains speech therapy.

**Conclusion** A growing body of research has attempted to uncover the pathophysiology of stuttering. Referral for speech therapy remains the best option for children and adults.

#### EDITOR'S KEY POINTS

- Stuttering is a common speech disorder that normally resolves by early adolescence. Developmental stuttering can be distinguished from typical disfluency of childhood by occasional prolongation of sounds and increased learned secondary behaviour, including closing the eyes or tensing facial muscles while stuttering.
- Stuttering is associated with psychosocial morbidity and worsened quality of life in adults.
- Medications, including atypical antipsychotics, might serve as an adjunctive treatment option for adults who stutter, but evidence is limited to small trials. Speech therapy performed by a specially qualified speech-language pathologist remains the mainstay of treatment at any age. Early intervention and referral for speech therapy in children is critical.



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Stuttering is a common speech disorder in persons of all ages that can cause disturbances in the normal fluency and time patterning of speech.<sup>1</sup> Developmental stuttering (DS)—stuttering that is inappropriate for the level of language development—is the most common form.<sup>2</sup> Current evidence suggests the disorder stems from inherited central nervous system abnormalities that disrupt fluent speech.<sup>3</sup>

The incidence of DS varies according to age group and the exact definition of *stuttering* used. A lifetime incidence (chance that an individual will ever stutter) of 5% is the most consistently reported statistic. However, recent data suggest a lifetime incidence closer to 10%,<sup>4,5</sup> with most of the burden in children. Up to 90% of children who stutter (CWS) will naturally recover during childhood. Adults who did not recover in childhood are said to have persistent DS, which is estimated to occur in less than 1% of the population.<sup>4</sup> Acquired forms of stuttering thought to be secondary to emotional trauma or brain damage are rarer, although exact estimates are unknown.<sup>6</sup> Males are 4 times more likely to have DS compared with females,<sup>4</sup> and DS is more likely to persist in males than in their female counterparts. Late age of onset, longer duration of stuttering, family history of persistence, and lower language and nonverbal skills are other predictors of persistence.<sup>7</sup>

Prompt diagnosis in children is critical, as early intervention yields the best outcomes.<sup>8</sup> Family doctors or pediatricians are often the first health care contact for CWS. For adults who stutter (AWS), physician knowledge of the causes, treatments, and

indications for referral can assure appropriate management in this population. In either case, a more robust understanding will better equip physicians, alongside speech pathologists, to identify stuttering and manage associated psychological issues.

### Quality of evidence

We reviewed the literature on DS by searching the MEDLINE and Cochrane databases for relevant articles on the epidemiology, genetics, pathophysiology, diagnosis, and treatment of the condition. We also reviewed the references of each article to ensure that we were including relevant articles that might not have been indexed by either of the databases. Last, we consulted with several experts in epidemiology, genetics, functional brain anatomy, and diagnosis of stuttering to ensure that we included all important data while keeping the review relevant and pertinent to primary care physicians. Most recommendations are based on small studies, limited-quality evidence, or consensus.

### Main message

**Pathophysiology.** There is no consensus on the pathophysiology of stuttering. Research exploring sensory, motor, and cognitive causes<sup>9</sup> has mostly yielded inconsistent or nonreproducible results. One consistent finding has been abnormal auditory feedback systems in persons who stutter (PWS).<sup>10</sup>

Neuroimaging studies have demonstrated differences in anatomy and function of the brain in CWS compared with fluent controls, specifically in auditory and motor regions and the basal ganglia.<sup>11</sup> These abnormalities might increase over time in individuals who do not recover from DS. Adults who stutter demonstrate hyperactivity of right hemispheric regions<sup>12,13</sup> and abnormal coordination between brain areas that plan and execute speech.<sup>14</sup> It is unclear whether anatomic and functional differences are a cause of stuttering or an adaptation to stuttering in the adult brain.

Dopamine dysregulation might also be a contributor. Levodopa administration increases disfluency,<sup>15,16</sup> while administration of dopamine antagonists has improved fluency.<sup>17-20</sup> One study using positron emission tomography showed increased uptake of the fluorinated dopamine precursor 6-FDOPA in PWS compared with controls,<sup>21</sup> suggesting hyperactivity of dopaminergic systems in the central nervous system.

**Genetics.** Since the 1930s, research has supported a genetic basis of stuttering. Familial studies have consistently shown that PWS are more likely than controls to have family members who also report a history of stuttering. A recent review<sup>4</sup> of 28 studies estimated that between 30% and 60% of PWS had a positive family history compared with less than 10% of controls. Twin studies have

confirmed these findings.<sup>22-24</sup> Additionally, male relatives carry a substantially higher risk than female relatives do.<sup>25-27</sup> Recovery and persistence appear to be distinct heritable conditions.<sup>28,29</sup>

Stuttering has been associated with changes on chromosomes 9, 10, 12, 13, and 18.<sup>30-34</sup> Genetic analysis of the DRD<sub>2</sub> gene, a prevalent dopamine receptor in the brain, showed increased frequency of a specific allele in AWS<sup>35</sup>; however, this finding was not replicated in a subsequent analysis.<sup>36</sup> Large association studies have identified 9 genes associated with stuttering, some of which were on chromosomes previously associated with stuttering.<sup>37</sup> Proposed functions of the identified genes include neurometabolism, cell-cell interaction, embryonic transcription regulation, and behaviour modification. Despite these promising results, clear mechanisms of actions have yet to be identified.

**Diagnosis.** Family physicians might be the first contact for parents of CWS, so knowledge of the types of disfluencies is important. **Table 1** outlines forms of early disfluency.<sup>38</sup> Normal disfluency, or disfluency that is not pathologic and that can be part of normal language development between the ages of 18 months and 7 years, can result in repetitions of sounds, syllables, or words.<sup>38</sup> Generally, after about 3 years of age, normal disfluency might cause the repetition of whole words or phrases (eg, "I want ... I want ... I want to go"). Such behaviour might increase when children are tired, upset, or being rushed, but it generally waxes and wanes, sometimes disappearing for months. Children with typical disfluencies do not notice or become frustrated by their speaking difficulties.

Children with DS, on the other hand, can be classified into categories based on the severity of stuttering. Children with mild stuttering, which can begin between 18 months and 7 years, show similar patterns of repetitions with greater frequency of disfluency. In addition to repetitions, children might occasionally prolong sounds ("Mmmm-ommy"). Nonetheless, it is often difficult to distinguish the mechanics of speech in children with normal disfluency from those with mild stuttering, so the presence of other secondary behaviour is helpful. Children with mild stuttering might begin to manifest secondary behaviour such as closing their eyes or tensing facial muscles during stuttering episodes. Children with mild stuttering might feel frustrated at times but are often not overly concerned.<sup>38</sup>

Children with severe stuttering, more common in later childhood, have speech disfluencies in many more speaking situations. These might include silent blockages of speech lasting 1 second or longer. Severe stuttering might produce more learned secondary behaviour, including eye blinks and looking away. Children with severe stuttering are frustrated and embarrassed, creating a potential

**Table 1. Forms of early disfluency**

VARIABLE	NORMAL DISFLUENCY	MILD STUTTERING	MODERATE TO SEVERE STUTTERING
Speech behaviour you might see or hear	Occasional (not more than once in every 10 sentences), brief (typically 0.5 s or less) repetitions of sounds, syllables, or short words (eg, li-li-like this)	Frequent (3% or more of words), longer (typically 0.5 to 1 s) repetitions of sounds, syllables, or short words (eg, li-li-li-like this). Occasional prolongations of sounds	Very frequent (10% or more of words), and often very long (1 s or longer) repetitions of sounds, syllables, or short words; frequent sound prolongations, and complete blocks (where little or no sound comes out)
Other behaviour you might see or hear	Occasional pauses, hesitations in speech, or fillers such as "uh," "er," or "um"; changing of words or thoughts	Repetitions (eg, "she-she-she") and prolongations (eg, "shshshe") begin to be associated with eye closing and blinking, looking to the side, and some physical tension in and around the lips	Similar to mild stuttering only more frequent and noticeable; some rise in pitch of voice during stuttering; more physical tension; extra sounds or words used as "starters"
When problem is most noticeable	Tends to come and go when child is tired, excited, talking about complex or new topics, asking or answering questions, or talking to unresponsive listeners	Tends to come and go in similar situations to those for normally disfluent children but is more often present than absent	Tends to be present in most speaking situations; far more consistent and nonfluctuating than for children with mild stuttering
Child's reaction	None apparent	Some children have awareness but little concern; some show frustration and embarrassment	Most are frustrated; some are embarrassed or fearful of speaking
Parent reaction	None to some concern	Most have at least some concern	All have some degree of concern
Referral decision	Provide handouts and Stuttering Foundation website ( <a href="http://www.stutteringhelp.org">www.stutteringhelp.org</a> ) and contact information. Make referral for evaluation if requested	Provide handouts and Stuttering Foundation website ( <a href="http://www.stutteringhelp.org">www.stutteringhelp.org</a> ) and contact information. Refer for evaluation if problem continues for 6–8 wk or parents request it	Provide handouts and Stuttering Foundation website ( <a href="http://www.stutteringhelp.org">www.stutteringhelp.org</a> ) and contact information. Refer for evaluation as soon as possible

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fear of speaking. This might lead to psychosocial impairment such as social anxiety; however, there is no evidence that severe stuttering is associated with learning disabilities or other behavioural problems. Severe stuttering is more likely to persist into adulthood.<sup>38</sup>

Adults who stutter tend to manifest similar patterns of speech disfluencies. Repetitions, prolongations, and silent blockages are common and can be disabling.<sup>39</sup> Secondary behaviour might be prominent. Techniques used to avoid challenging words, such as substitution, can be deep-rooted. Adults who stutter show wide variation in their degree of frustration with speaking.<sup>40–42</sup>

**Psychosocial morbidity.** Social and generalized anxiety have shown robust positive associations with stuttering, theorized to be a result of the cumulative negative social effects of stuttering.<sup>43,44</sup> While the relationship between stuttering and anxiety is inconclusive in children, there is good evidence supporting the relationship in adolescents, young adults, and older adults.<sup>45</sup>

The evidence suggests that most CWS do not show increased anxiety until adolescence, although conclusions are limited by the heterogeneity of studies in this

area.<sup>46,47</sup> One theory suggests that CWS experience negative environmental risk factors beginning in early childhood, including negative experiences of socialization, which coalesce during adolescence, a time of greater social and physical change.<sup>46</sup> A study of adolescents who stutter aged 12 to 17 concluded that 38% qualified for at least 1 mental disorder according to *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, criteria; anxiety was the most prevalent.<sup>48</sup> In that study, older adolescents aged 15 to 17 reported significantly greater anxiety ( $P=.010$ ) and emotional and behavioral problems ( $P=.036$ ) compared with adolescents aged 12 to 14, although mean scores were normal in both groups. Stuttering in adults, on the other hand, has been associated with 2-fold increased odds of any mood disorder<sup>49</sup> and 3-fold higher odds of personality disorders compared with matched controls.<sup>50</sup>

Stuttering in adults has also been associated with lower quality of life, occupational and educational burdens, and barriers to receiving high-quality health care.<sup>51,52</sup> In a survey of AWS, more than 70% agreed that stuttering decreased the chance of being hired or receiving promotions, and 68% reported that stuttering had interfered with

their job performance.<sup>53</sup> In addition, self-reported stuttering severity was negatively related to highest educational achievement.<sup>54</sup> A recent qualitative study found that AWS sometimes avoided medical interactions or avoided discussing sensitive topics with their physicians.<sup>55</sup>

### Treatment

**Pharmacologic:** With increasing knowledge of the pathophysiology of stuttering, pharmacologic management of stuttering has received attention.<sup>56,57</sup> Clinical trials have primarily evaluated antidepressants, anxiolytics, and antipsychotics. Evidence supporting use of these agents is limited.<sup>58</sup>

Antidepressants have not shown a clear benefit. The selective serotonin reuptake inhibitor paroxetine was not associated with a significant change in fluency.<sup>59</sup> The tricyclic antidepressants clomipramine and desipramine showed minimal short-term improvements in some measures of fluency and decreases in self-reported speaking avoidance compared with placebo in a trial of 16 participants<sup>59,60</sup>; a separate analysis showed clomipramine to be superior to desipramine on self-report scales on fluency.<sup>60</sup> However, neither manuscript provided long-term data.

Despite the association between anxiety and stuttering, few trials have measured the effect of anxiolytics. Data on benzodiazepine efficacy, in particular, are limited. A noncontrolled trial of 3 participants taking a combination of an antidepressant and alprazolam showed marked improvement in stuttering severity scores.<sup>61</sup> More recently, pagoclone, a novel non-benzodiazepine  $\gamma$ -aminobutyric acid modulator, was tested in the largest randomized controlled trial of stuttering.<sup>57</sup> Despite a promising 4-fold reduction in stuttering in phase IIa studies, results from phase IIb studies have yet to be published, and the company terminated future research.<sup>62</sup>

Antipsychotics that block dopamine receptors in the brain have shown promising results, but much of the data are not easily replicable, are older, or are limited to small studies. Haloperidol was first tested in 1971 in a randomized trial of 36 participants and showed remarkable results: a reduction from 50.8% disfluencies to 9.7% after 8 weeks.<sup>63</sup> Subsequent studies have inconsistently replicated these findings, and treatment has been associated with substantial side effects. Based upon a stringent set of criteria, a recent systematic review concluded that the positive effect of haloperidol on stuttering symptoms is not supported by the literature.<sup>58</sup> The atypical antipsychotic risperidone showed significant improvements in stuttering at 6 weeks compared with both placebo and baseline ( $P = .025$ ).<sup>19</sup> Olanzapine, another atypical antipsychotic, showed a statistically significant effect on stuttering symptoms compared with placebo in a randomized trial of 24 participants,<sup>20</sup> with the primary side effect

being weight gain. Neither of these studies assessed long-term effects. Case studies have documented successes in treating stuttering using asenapine, a newer atypical antipsychotic, but there are no controlled studies yet.<sup>64</sup>

**Nonpharmacologic treatments and speech therapy:** There is minimal high-quality evidence available testing the efficacy of nonpharmacologic treatment of stuttering. Acupuncture,<sup>65</sup> electromyography feedback of activity in lip muscles,<sup>66</sup> and delayed auditory feedback<sup>67</sup> have been examined in small studies with varying rates of success. A recent review<sup>56</sup> was unable to make any definitive recommendations for specific nonpharmacologic treatments.

Speech therapy performed by a specially qualified speech-language pathologist remains the mainstay of treatment. Such treatment differs substantially for children and adults. Treatment of children has shifted in the past 20 to 30 years from a "hands-off" attitude to more aggressive intervention.<sup>68</sup> Consensus is that early intervention with children is key, although there is debate about the preferred approach.<sup>8</sup> Multifactorial treatment strategies are the dominant paradigm in North America, and emphasize treating the child, identifying his or her stressors, and modifying environmental stressors starting from preschool. In contrast, the Lidcombe Program uses operant conditioning techniques to teach parents to verbalize positive and negative responses to their child's speech.

Treatment of adults has historically focused on stuttering management and speech restructuring. Stuttering management treats cognitive and behavioural issues associated with stuttering, particularly to relieve anxiety about speaking and stuttering. One randomized controlled trial of cognitive behavioural therapy performed by speech therapists showed decreased social anxiety and psychological distress in AWS.<sup>69</sup> Speech restructuring teaches new speech patterns, the most common of which is *slowed speech*, or controlling and slowing the rate of speech. Some newer intensive programs, such as that at the Hollins Communications Research Institute in Virginia, combine both approaches. Efficacy data on these intensive programs are limited.<sup>56</sup>

### Conclusion

Developmental stuttering is a common speech disorder that normally resolves by early adolescence. Persistent forms are rarer and are associated with psychiatric and social morbidity. **Table 2** summarizes the key recommendations for practice.<sup>7,35,40,41,48,49,55,63</sup> A growing body of genetic, neurologic, and theoretical research has provided insight into the pathophysiology of stuttering, but there is no consensus to date. Pharmacologic treatments have received attention, but further research is

**Table 2. The SORT for key recommendations for practice: B recommendations are based on inconsistent or limited-quality patient-oriented evidence; C recommendations are based on consensus, usual practice, opinion, disease-oriented evidence, or case series.**

CLINICAL RECOMMENDATION	EVIDENCE RATING	STUDIES
Stuttering can be distinguished from typical disfluency of childhood by the occasional prolongation of sounds and increased learned secondary behaviour, including closing the eyes or tensing facial muscles while stuttering	C	Lan et al <sup>35</sup>
Stuttering is associated with psychosocial morbidity and worsened quality of life in adults	B	Corcoran and Stewart, <sup>40</sup> Crichton-Smith, <sup>41</sup> Gunn et al, <sup>48</sup> and Iverach et al <sup>49</sup>
Medications, including atypical antipsychotics, might serve as an adjunctive treatment option for adults who stutter, but evidence is limited to smaller trials	C	Perez et al <sup>55</sup>
Early intervention and referral to speech therapy in children who stutter is critical	C	Yairi et al <sup>7</sup>
Speech therapy is the mainstay of treatment for stuttering in children and adults	C	Wells and Malcolm <sup>63</sup>

SORT—Strength of Recommendation Taxonomy.

needed. Speech therapy remains the treatment of choice, and early intervention is critical in CWS. 🌿

Dr Perez is Assistant Professor in the Department of Medicine at Albert Einstein College of Medicine in New York, NY. Mr Stoeckle is a fourth-year medical student at Tulane University School of Medicine in New Orleans, LA.

#### Contributors

Both authors contributed to the literature search and interpretation, and to preparing the manuscript for submission.

#### Competing interests

None declared

#### Correspondence

Dr Hector R. Perez; e-mail [heperez@montefiore.org](mailto:heperez@montefiore.org)

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